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Abstract

Background: Patients with new onset constipation or presumed hemorrhoid bleeding frequently require the use of both fiber supplements and diagnostic colonoscopy. We sought to determine whether preliminary fiber supplementation would alter the tolerability or efficacy of a standard bowel preparation for colonoscopy

Methods: A prospective, double blind, randomized trial was designed to compare a short course of a psyllium-based supplement versus placebo prior to a colon lavage. Patients were given an unlabeled canister of powder, and instructed to take 1 tablespoon with 8 oz of water bid for 4 days before colonoscopy. A 4-liter polyethylene based glycol lavage was self-administered over 4 hours on the day prior to colonoscopy. A questionnaire on pre-study bowel habits and side effects was completed. Efficacy of the preparation was visually evaluated on a pre-determined scale.

Results: There were no significant differences between the two groups in gender, race, age, pre-study stool frequency or consistency. Tolerability was equivalent but efficacy of the bowel preparation was worse in the psyllium group compared to placebo ($P < 0.05$).

Conclusions: In non-constipated patients psyllium based fiber supplementation should not be initiated in the few days prior to endoscopy using a polyethylene glycol preparation.

Background

Colorectal cancer is the second leading cause of cancer mortality in the US with an estimated 150,000 new cases expected to be diagnosed in 2003 [1]. The recognition that prompt diagnosis and removal of neoplastic polyps is associated with decreased colorectal cancer mortality has stimulated more aggressive screening. Increasing public awareness and the availability of reimbursement for screening colonoscopy may further increase the number of screening colonoscopies performed. In addition, the typical Western diet is notable for a relative deficiency in dietary fiber, and a high prevalence of colon disorders including irritable bowel syndrome, diverticulosis (with or without diverticulitis), neoplastic polyps, cancer and a myriad of anal disorders. Many of the symptoms or signs related to these disorders also prompt screening for colorectal cancer or other significant colonic pathology.

Adequate bowel preparation is critical to colonoscopy, as a poor preparation may obscure pathology or prevent full colonoscopy. Rex at al. estimated that unsuccessful colonoscopy leads to second procedures in up to 20% of patients [2]. Most colonoscopists advise the patient to eschew fruits and vegetables for some period of time prior to colonoscopy because large undigested fragments of these foods may remain in the colon and obscure the bowel. However, the need to avoid powdered fiber supplements, which consist of much smaller particles, is less clear. Indeed, dietary or supplemental fiber is an essential element of colon health and bulk transit of stool. McRorie described a new objective measure "Stool Viscosity Ratio", a ratio of highest stool viscosity to lowest stool viscosity [3]. This was useful in explaining the origin of High Amplitude Propagating Contractions, motor activity of the colon felt to be primarily responsible for cramping pains when high volume luminal liquid meets solid stool. Since cramping is felt to be a major component of discomfort during colon preparation [4], it was hypothesized that pre-treating the colon with a stool-softening fiber supplement could reduce cramping and improve tolerability. More importantly, since many patients requiring colonoscopy may also benefit from fiber supplementation, either because of hemorrhoidal problems or constipation, we sought to determine whether fiber supplementation in the fiber-naïve patient might alter the quality of the bowel preparation, either from direct mechanical effects of the fiber on the stool or from changes in tolerability and compliance with the preparation.

We therefore sought to determine whether starting fiber supplementation prior to colonoscopy might affect the tolerability or efficacy of a standard polyethylene glycol based lavage preparation for colonoscopy. We established a randomized double blind trial in which consenting patients received either powdered psyllium or a placebo control twice daily for four days prior to large volume polyethylene glycol preparation and colonoscopy. We then compared the discomfort produced by the preparation and the adequacy of bowel preparation at colonoscopy in these two groups of patients.

Methods

Patients

After approval by the Institutional Review Board of Wayne State University, eligible patients were offered trial participation. Patients were eligible if they were scheduled to undergo elective colonoscopy for screening or symptom evaluation and could comply with required procedures. Patients were excluded for chronic laxative use, chronic use of fiber supplements, swallowing difficulties, known or suspected bowel obstruction, prior colon resection, allergy to psyllium or aspartame, or diabetes.

Study design

Following informed consent, patients were entered into a prospective, randomized, double blind trial of psyllium powder (sugar-free Metamucil®, Procter & Gamble, Mason, Ohio) versus placebo (Tang®, Kraft Foods, Northfield, Illinois) as an adjunct to bowel preparation for colonoscopy. Patients were seen by the research pharmacist and randomized equally between the two groups using pulled cards. Patients were assigned to either psyllium or placebo, 1 heaping tablespoon BID with a full 8 ounces of water for four days prior to colonoscopy. The fiber content in the psyllium arm was approximately 20 grams per day, based on 3.4 grams of fiber per teaspoon. The patients were provided with an unlabeled canister, which was returned to the pharmacy for weight determination on the day of colonoscopy. A low bulk fiber diet was prescribed for the duration of the study. A study nurse was in contact with patients over this time to improve compliance and completion of the study. On the day prior to colonoscopy each patient was advised to consume a standard four-liter polyethylene glycol based electrolyte solution (PEG-3350 & electrolytes for oral solution, Colyte®, Schwarz Pharma, Milwaukee, Wisconsin) over 3–4 hours. On the day of colonoscopy, each patient underwent a structured interview that included questions rating pre-preparation bowel habits such as frequency (bowel movements per day or week), consistency (a visual analog scale from 1–7, watery to hard and difficult to pass), and the number of minutes per day spent attempting to defecate. Compliance with the regimen (diet, PEG-3350, and powder) was self-reported as a fraction from non-compliant to fully compliant. Medication canisters were weighed prior to distribution and upon return to further assess compliance. Tolerability of the four-day regimen (first hour of lavage, full volume of lavage, and overall tolerability of the regimen) evaluating bloating, gas, cramping, urgency, nausea and heartburn was assessed using a previously published visual analog scale from 0 (none) to 5 (extreme) [3]. During colonoscopy, a surgical endoscopist not involved in the endoscopy itself observed the entire procedure and assessed the quality of bowel preparation based on the worst portion of the exam using a scale of 1–7 to facilitate data analysis (Table 1). Subjective observations on the bowel preparation were permitted in addition to the overall score. Volume of irrigation was recorded as part of the score. Patient, endoscopist, and observer were all blinded to the study medication throughout the study and the blind was only broken after all patients had completed the research study.

Statistical analysis

A preliminary power calculation utilized quality of the bowel preparation as the primary endpoint for this study, since an improvement in tolerability would not be considered as important as a change in efficacy of the

Table 1: Grading of Bowel Preparation

1.	Clean mucosa ± occasional liquid stool
2.	Clean mucosa with <100 cc liquid stool
3.	Clean mucosa with 100–300 cc liquid stool
4.	Clean mucosa with >300 liquid stool or small amounts of formed stool
5.	Moderate amount of formed stool – mucosa still evaluable
6.	Moderate to large amount of formed stool – mucosa not fully evaluable
7.	Unable to reach cecum secondary to formed stool
8.	Unable to reach cecum for technical reasons unrelated to the prep.

preparation. We sought to find a difference in the mean quality of bowel preparation (based upon our previously established scale) of 1.0, and hypothesized based upon previous pilot experience developing and validating the scale that the standard deviation of this data would also be 1.0. With a sample size of 20 in each group, this yielded an estimated power of 0.869 for the study as designed, which we considered acceptable. Validity of randomization for age, gender, stool frequency, consistency, time spent attempting to defecate, and compliance with the regimen was assessed using Chi-square analysis for discontinuous variables or proportions and students T-test assuming unequal variance for continuous variables. Differences in tolerability between the regimen with the active fiber supplement and that with the placebo were assessed by comparing the mean score for each symptom at each time point by two-tailed T-test assuming unequal variance. Efficacy was compared using the two-tailed T-test assuming unequal variance. Statistical significance was established *a priori* at $P < .05$. Results for continuous variables are presented as X ± SD.

Results

64 patients initially consented and enrolled in the study. 24 patients were subsequently excluded from being analyzed. Ten patients chose not to undergo colonoscopy after initially consenting to the procedure. Eleven patients withdrew from the study after receiving their assigned canister and underwent colonoscopy without powder supplementation. Two patients were excluded because they did not consume at least 75% of the colyte solution, and one patient was removed for self-prescribing a laxative during preparation. All information leading to exclusion was ascertained prior to colonoscopy. The 24 patients excluded were equally divided between the two test powders (12 psyllium and 12 placebo). Of the 10 patients not undergoing colonoscopy, 6 were initially randomized to the placebo group and 4 to the psyllium group. Of the 11 patients withdrawing, 5 were initially randomized to psyllium and 6 to the placebo arm.

This left 40 fully evaluable patients, with 20 allocated to each of the two groups. Thirty-nine of 40 patients were male, consistent with the Veterans Administration Hospital population. Mean age in the psyllium and placebo groups was 60.4 ± 9.6 years and 61.4 ± 10.9 years respectively. Eighty percent of the psyllium patients and 85 percent of the placebo group had a stool frequency of "daily" or more frequently. Stool consistency was self-reported on the 1–7 scale as 4.3 ± 1.1 for psyllium and 4.0 ± .8 for the placebo group. Self-reported time at stool for each bowel movement for the psyllium group was 8.8 ± 7.8 minutes and for placebo 7.1± 6.9 minutes. Median and modal values for time at stool were significantly lower than the mean, but there was no difference between psyllium and placebo. Median time was 5–6 minutes and the mode 2–3 minutes indicating a skewed distribution secondary to prolonged defecating times reported by a minority of "readers". Compliance with a low fiber diet was described as "mostly" (20%), or "completely" (75%) in both groups. Self-reported compliance with powder consumption in the psyllium group was "no missed doses" (70%) "missed one dose" (20%), and "missed two doses" (10%). Comparative compliance in the placebo group was 75%, 15%, and 10% respectively. By canister weight, the powder consumed in the psyllium group was 80.1 ± 26.7 grams with an expected consumption of 88 grams. There were no significant differences between the psyllium and placebo groups with respect to gender, race, pre-preparation bowel frequency, stool consistency, time defecating, or compliance with the prescribed regimen (diet, PEG-3350, or powder).

No significant differences were found in tolerability of the two regimens for bloating, gas, cramping, urgency, nausea, or heartburn assessed during the first hour of PEG-3350 lavage, full volume of PEG-3350 or overall. Scores for each of the symptoms varied widely with a near zero incidence of nausea or heartburn. Most patients reported minimal to no discomfort, with only a mild sense of bloating and urgency; however these were the only side effects for which several patients recorded a score of 5 (extreme). Two of the 40 patients described extreme (5/5) cramping with the full volume of lavage, but all other patients reported minimal or no cramping (2 or less).

The cecum was reached in 18 of 20 in the psyllium group and 19 of 20 in the placebo group. This difference was not statistically significant. However, the quality of bowel preparation was significantly worse in patients receiving psyllium. The bowel preparation for the psyllium group was scored as 3.8 ± 1.39 (X ± SD). In contrast, bowel preparations of patients taking the placebo were scored as 2.6 ± 1.4 (X ± SD). This difference was statistically significant by T test assuming unequal variances. (N = 20, p = 0.009). No attempt was made to independently score individual anatomic segments of the colon. Review of subjective comments beyond the bowel preparation scores by the blinded observer after the double blind had been broken were remarkable only for the observation that two patients in the psyllium group were noted to have an unusual fecal coating or "paste-like" appearance in the right colon. This was not described in any patients in the placebo group.

Discussion

Colonoscopy remains the gold standard to evaluate the colonic mucosa. Several pre-colonoscopy bowel preparation regimens exist, but none has emerged as clearly superior. In all these regimens, patients are generally asked to avoid fruit and vegetable intake as much as possible for some period of days prior to colonoscopy because large undigested pieces of vegetable fiber could interfere with complete visualization of the mucosa. The introduction of a polyethylene glycol (PEG) based colon lavage in 1980 [5] has minimized the fluid and electrolyte problems associated with potent hypertonic cathartics. However, patients frequently find the large volume of liquid difficult to tolerate, leading to non-compliance and inadequate preparation. Many investigators have therefore continued to study sodium phosphate preparations with varying results [4,6-9]. Others have attempted to circumvent the volume problem by combining varying doses of the stimulant laxative bisacodyl with a lower volume PEG-based lavage [10].

Residual feces after poor bowel preparation may obscure lesions or even prevent completion of the procedure. Repeat bowel preparation and additional testing after incomplete procedures places additional burdens upon the patient and the health care system, while the cost of missed lesions is obvious. Providing an effective and well-tolerated bowel preparation is thus desirable.

This study attempted to improve tolerability and efficacy of a standard PEG preparation with a short preliminary course of a psyllium-based powdered fiber. This study failed to demonstrate any improvement. In fact, psyllium impaired bowel preparation. Several possibilities exist for decreased efficacy, including continuing fiber supplementation on the day of lavage, the adhesion of small particles of fiber and stool to the mucosa or non-compliance with adequate water intake, which was not measured. Whether these findings are relevant for chronically constipated patients who are already dependent on chronic fiber supplementation cannot be answered by this study.

In this group of non-constipated patients, who generally self-rated their stool consistency as midway between liquid and hard, moved their bowels daily or more often, and spent a median time at defecating of 5–6 minutes, the cramping pains associated with high pressure contractions as hypothesized by McRorie [3] did not seem highly prevalent during a PEG lavage preparation and were not influenced by use of psyllium powder. Urgency during the 4-hour lavage phase was the most notable side effect of the bowel preparation but was expected to some extent by all patients and thus may have been under-reported. Bloating was the second most frequent side effect and generally mild.

The use of a dietary powdered fiber preparation is well established for a myriad of colorectal problems, including constipation, anal fissures, symptomatic hemorrhoids, and recurrent diverticulitis. Fiber may also facilitate cholesterol control. Colonoscopy requires a well-prepared colon to reduce the need for premature repeat testing or the requirement for additional diagnostic tests. This study suggests that powdered fiber supplementation should not be initiated within a few days before a colon lavage preparation for colonoscopy. Although fiber supplementation is clearly effective for hemorrhoidal disease, patients presenting with presumed hemorrhoidal bleeding should either receive colonoscopy first or the endoscopist may wish to consider stopping the fiber supplement several days prior to colonoscopy if a PEG-based preparation is to be used. The impact of fiber on a sodium phosphate preparation is unknown, but might be speculated to be similar. Patients suffering from significant constipation may represent a distinct cohort requiring individualized treatment.

Nearly 37% of initially randomized patients failed to complete the study. Patients withdrawing after initial consent were not pursued or formally questioned regarding their decision to withdraw since the primary endpoint of the study was efficacy of bowel preparation and not tolerability. However, the number of patients failing to complete the study was equally distributed between the two groups, suggesting that the side effects of either medication were probably not responsible for self-removal from the study. The "no show" or cancellation rate for colonoscopy at the study facility outside of research is approximately 25% from all causes. In this limited study, patients were not stratified by their indication for endoscopy. However, others have not found this to be an independ-

Table 2: Demographics of Study Population

	Psyllium	Placebo	Significance
Age	60.4 ± 9.6	61.4 ± 10.9	Ns
Stool Consistency	4.3 ± 1.1	4.0 ± .8	ns
Stool Frequency			ns
Weekly	0	1	
Every other day	2	1	
Occ. skip days	2	1	
Daily	12	10	
Twice daily	3	6	
More than bid	1	1	
Compliance			
With diet			ns
Complete	15/20	15/20	
Partial	4/20	4/20	
Not Compliant	1/20	1/20	
With powder			ns
Complete	14/20	15/20	
Missed 1 dose	4/20	3/20	
Missed 2 doses	2/20	2/20	

Table 3: Efficacy and Tolerability of Bowel Preparation

	Psyllium	Placebo	Significance
Cecum	18 /20	19 /20	ns
Quality	3.8 ± 1.39	2.68 ± 1.4	P=.009
Tolerability*			
Bloating	1.75 ± 1.6	1.1 ± 1.3	ns
Gas	1.7 ± 1.45	1.1 ± 1.0	ns
Cramping	0.5 ± 1.5	0.35 ± .81	ns
Urgency	2.4 ± 1.8	2.6 ± 1.53	ns
Nausea	0.15 ± 0.6	0.1 ± .44	ns
Heartburn	0 ± 0	0.25 ± .78	ns

* Worst mean score (0–5) for any of three time periods, (First Hour, Full Lavage, Overall)

ent variable for efficacy in bowel preparation [10]. A uniformly accepted scale for both tolerability and efficacy would enhance comparison between divergent strategies.

Conclusions

Psyllium based fiber supplementation does not significantly improve tolerability of a lavage based preparation for colonoscopy and when provided within several days of colonoscopy may impair visualization. At least in non-constipated patients fiber supplementation should be discontinued prior to a lavage based preparation for colonoscopy, and patients who require both colonoscopy and a prescription for fiber supplementation should receive colonoscopy prior to starting fiber supplements.

Competing interests

Dr. Marc Basson received partial research funding for this study from Procter & Gamble and has previously received research funding from Procter & Gamble for other experimental studies. Dr. Salwen has no competing interests.

Authors' contributions

MDB conceived of the study, participated in conduct and oversight of the study, performed statistical analysis and assisted in manuscript preparation WS recruited patients, served as blinded observer, maintained the database and drafted the manuscript

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